

REMARKS

These remarks are in response to the Office Action dated February 22, 2010. Applicant respectfully requests a three month extension of time. Authorization is given to charge the appropriate fees to Deposit Account No. 50-0951.

At the time of the Office Action, claims 1-14 were pending. Claims 1-5, 9-12 and 14 were withdrawn in a previously issued Restriction Requirement. In the Office Action, claims 6-8 and 13 were rejected under 35 U.S.C. §103(a). The rejections are discussed in more detail below.

I. Rejections to the claims based upon Art

Claims 6-8 and 13 were rejected under 35 U.S.C. §103(a) as unpatentable over the article to Hatzinikolaou et al. ("*Hatzinikolaou*") in view of U.S. Patent No. 3,992,262 to Shieh ("*Shieh*") and U.S. Patent No. 3,625,826 to Kobayashi ("*Kobayashi*").

Applicant respectfully traverses these rejections, and disagrees with the Examiner for the following reasons.

First, the paper by *Hatzinikolaou* relates to the optimization of the production of glucose oxidase by fungi, in particular *A. niger*, using low-cost carbon sources. It is known to the person of ordinary skill in the art that the optimal conditions of production of enzymes, acids, and other such products from a microbial fermentation do not necessarily correspond to the optimal growth conditions of the microorganism itself. Therefore, the optimization of the production of glucose oxidase reported in this paper cannot be necessarily interpreted as the achievement of the optimization of the growth conditions of the fungi itself. This is confirmed by a statement on page 531, end of first paragraph of the section under the heading "Effect of carbon source", where it is stated that no correlation between biomass production and enzyme activity could be established. Therefore, the skilled person would not have looked into this document for optimizing growth conditions of the fungi. Had s/he done so, s/he would have found no useful teaching therein.

In *Hatzinikolaou*, various carbon sources are separately tested. In fact, molasses and sucrose are never combined. Therefore, a composition that is the same as that of the medium

recited in the present claims is never tested and no mention or hint is given pointing towards combining the carbon sources.

Figure 2 shows that the greatest enzyme activity was achieved using molasses, followed by sucrose. Also see page 531 of *Hatzinikolaou*, last but one paragraph, where it is stated that molasses gave the highest yields of enzyme activity and was chosen as the main carbon source, while sucrose was only used as a reference (also see page 532, first paragraph of the right hand side column). Table 1 shows that lactose gives the best results for biomass production. The skilled person, based on these teachings, would have found no reason to combine the molasses with sucrose. The paper effectively teaches against the use of both molasses and sucrose in the same medium.

As for the nitrogen source, best results in combination with molasses are described as being given by urea and NaNO_3 for biomass production, and by peptone and NaNO_3 for enzyme activity (Table 2). Peptone is the nitrogen source of choice (column 2 of page 532, lines 1-4). The paper thus teaches against the use of corn steep liquor and yeast extract, as they give poorer results by comparison, and even more so to the combination thereof.

To summarize, *Hatzinikolaou* is not related to the technical problem of the present application and in any case contains no teaching pointing towards the medium composition of the present claims. In fact, in many respects, it teaches away from the present claims.

Turning now to the patent by *Shieh*, it must be pointed out that this patent relates to bacteria, not fungi. There are no fungi disclosed in this document. All the genera listed in column 2, lines 3 to 11 of D1 are bacterial genera. The skilled person would thus not have looked into this document as it is well known that bacteria and fungi have different growth requirements.

Had the skilled person consulted *Shieh*, however, s/he would have found no useful teaching. The technical problem solved by *Shieh* is that of providing a method for growing such bacteria using a medium which is relatively inexpensive and which results in a good yield of production of the enzyme glucose isomerase. The problem is solved by a method of producing glucose isomerizing enzyme in a medium comprising molasses, corn steep liquor and an inorganic nitrogen salt (column 1, lines 60 to 64). No yeast extract is included in the composition. This is not related to providing a culture medium for filamentary fungi that allows such microorganisms to be produced at industrial level at high yields in short periods of time.

As already mentioned above, the skilled person knows that the environmental conditions that are optimal for the production of an enzyme (or an acid, or other such product) from microbial fermentation are not necessarily the same as those associated to optimal growth of the microorganism itself. This statement is further confirmed in column 4, lines 60-65 of *Shieh* where it is stated that corn steep liquor promotes the production of the enzyme, whereas molasses stimulates the growth of the organism, which underlines the complexity of microbial metabolism and biochemistry. It is thus quite clear that the technical problem of *Shieh* is quite distant from that of the present application.

In any case, the skilled person would have found in *Shieh* no indication towards the medium composition of the present claims. *Shieh* states that the combination of molasses and corn steep liquor increases the production of the enzyme (column 4, lines 63-65). But the present composition is not directed to the production of enzyme, but to improved fungal growth. The skilled person would learn from *Shieh* to include molasses, but not corn steep liquor, in the medium. This document, therefore, also teaches away from the present claims.

The skilled person starting from *Hatzinikolaou* and wishing to improve the growth conditions of the fungi from the teachings of *Shieh*, in fact, would have chosen to exclude corn steep liquor from the composition, as this is particularly correlated to enzyme production and not to growth and, in fact, it is said to inhibit growth above a certain concentration (column 4, line 66 to column 5, line 1). Moreover, the nitrogen source of choice would have been urea, NH_4Cl , or NaNO_3 , and no yeast extract would have been included, as this latter nitrogen source is not even mentioned in *Shieh*.

The combination of *Hatzinikolaou* and *Shieh* could thus not lead to the present claims.

Turning now to *Kobayashi*, this document relates to improvements in a process for producing spiculisporic acid and a hydroxyl-acid form thereof, from the fermentation of *Penicillium spiculisporum* in a culture medium.

Again, the problem addressed in *Kobayashi* is completely different from that of the present application, as it relates to the production of acid by the microorganism, and not to the optimization of the growth of the microorganism itself. In lines 1 to 3 of column 2 of *Kobayashi*, it is stated that the pH during fermentation should remain as low as 1.2 to 2.5 (from a starting pH before fermentation of between 10 and 7.0, see column 3, lines 37-40). The pH in the culture broth

is said to have very great effects on the yield of the product (column 4, lines 1-3 of *Kobayashi*). Quite to the contrary, in the present culture medium, as shown in Example 4, the pH increases during fermentation, rather than decreasing. Although the pH value of the medium of the present application is not claimed, this observation is useful to underline that the composition and/or the use of medium of *Kobayashi* are clearly very different from those of the present application, to the point that the subject matters can be considered to be unrelated.

In column 3, lines 14 to 26 is provided a list of carbon and nitrogen sources without mention to any preference or functionality. The culture media composition described in the last paragraph of column 3 and in all the Examples of *Kobayashi* are different from that of the present application (no molasses, no yeast extract). Therefore, there is nothing in this document that adds any useful information to the skilled person in the direction of the present invention.

The skilled person would not have looked into this *Kobayashi* for solving the problem set out in the present application, as it relates to the optimization of the production of an acid from fungi. Had s/he done so, s/he would have found no useful teachings and, in fact, teachings that would have been contradictory with respect to his/her task, as the case turns out to be.

A person of ordinary skill in the art would have thus found no reason to look into any of the documents cited. Had s/he done so, however, s/he would have found no reason to combine their teachings, given that they solve different technical problems using different microorganisms for the production of different products.

Nevertheless, even if, as the Examiner suggests, the skilled person combined *Hatzinikolaou*, *Shieh* and *Kobayashi*, they would in fact prepare one of the culture media of the prior art and, if they inoculated it with the fungi of the present application, they then would need to attempt to contrast the rise in pH with an acid, to bring the medium down to a pH of about 2. This would not solve the technical problem of the present application and the composition of the medium would, in any case, be different from that claimed. The combination of these three documents thus fails to direct the skilled person towards the media composition of the present claims, as already discussed.

For the above reasons, the subject matter of claims 6 and 13 are patentable over the cited prior art. Similar arguments apply to dependent claims 7 and 8, which are believed to be allowable because of their dependence upon an allowable base claim, and because of the further features

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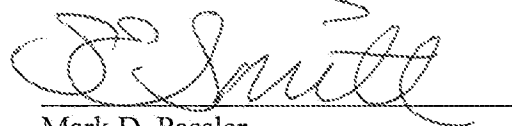
recited. All claims are thus believed to relate to patentable subject matter, and to be in condition for allowance.

II. Conclusion

Applicants have made every effort to present claims which distinguish over the prior art, and it is thus believed that all claims are in condition for allowance. Nevertheless, Applicants invite the Examiner to call the undersigned if it is believed that a telephonic interview would expedite the prosecution of the application to an allowance. In view of the foregoing remarks, Applicants respectfully request reconsideration and prompt allowance of the pending claims.

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